ABSTRACT

THESIS: Investigating the role of hypoxia on sinus venosus- and endocardial-derived coronary angiogenesis.

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Coronary artery disease kills seven million people every year. Understanding how coronary vessels develop when it is first formed in the embryo can help facilitate the design of therapeutics to repair and regenerate damaged coronary vessels in adults. Studies in mouse embryos show that coronary vessels arise from the endocardium and sinus venosus. Furthermore, a previous study revealed that endocardial coronary angiogenesis occurs in the hypoxic regions of the heart, whereas coronary angiogenesis from the sinus venosus occurred in non-hypoxic regions of the heart. However, it is unclear whether hypoxic cues promote inward growth of sinus venosus-derived vessels in the myocardium. This study aimed at characterizing the role of hypoxia in coronary vessel growth from its dual progenitor pathways. In particular, we investigated the role of hypoxia signals in the growth of coronary vessels from sinus venosus and endocardium in the myocardium. We utilized gain-of-function experiments *in vivo* using a mouse model and *in vitro* explant culture systems to interrogate the role of hypoxia in coronary angiogenesis. We hypothesized that myocardial hypoxia stimulates coronary angiogenesis from endocardium and promotes myocardial expansion of SV-derived vessels. Our results show that hypoxia positively impact the myocardial growth of coronary vessels from its dual progenitor population.